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Incidence of adult respiratory distress syndrome in trauma patients: A systematic review and meta-analysis over a period of three decades

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BACKGROUND: In trauma patients, acute respiratory distress syndrome (ARDS) is associated with high morbidity and mortality. Changes in diagnostics, management, and treatment may have influenced the incidence of ARDS. Therefore, the purpose of this article is to evaluate whether there is a difference in the incidence of posttraumatic ARDS (1) over time, (2) attributable to geographic distribution, and 3) related to admitting surgical subspecialities.

METHODS: A comprehensive search of articles published in English and German language was conducted using PubMed, MEDLINE, and the ISI Web of Science. Search terms included ARDS, acute respiratory distress syndrome, multiple trauma, polytrauma, and surgery. A meta-regression was performed to analyze differences between several decades of patient recruitment (decade 1, 1981–1990; decade 2, 1991–2000; decade 3, 2001–2010), geographic location (North America and Europe), and the type of admitting surgical service (general vs. orthopedic trauma), respectively. Statistical analyses were performed with R (version 3.1.2, metafor package).

RESULTS: The search included studies between January 1, 1980, and December 31, 2015 and revealed 43 trials from 40 publications (117,951 patients, 7,816 with posttraumatic ARDS). The median incidences over the last three decades were similar between decade 1 (10.4%), decade 2 (7.7%), and decade 3 (8.0%) ($p = 0.8322$). Geographical observations comparing central Europe and North America revealed no statistically significant difference (Europe 13.0%) and North America (6.9%), ($p = 0.0696$). The ARDS incidence in patients published based on a general surgery service (9.8%) was comparable to those published by orthopedic trauma surgeons (7.0%) ($p = 0.3436$).

CONCLUSION: The results of this meta-analysis discard the assumption that the following factors have influenced the incidence of posttraumatic ARDS: There was neither a change in the incidence over the last decades, nor a geographical difference within western societies, nor associated with the admitting surgical subspeciality. (*J Trauma Acute Care Surg.* 2017;83: 496–506. Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.)

LEVEL OF EVIDENCE: Systematic review, level III.
KEY WORDS: ARDS; trauma; incidence; meta-analysis; systematic review.

Acute respiratory distress syndrome (ARDS) continues to represent an important contributing factor towards morbidity and mortality after trauma.[1] The etiology of ARDS in trauma patients is heterogeneous. Both, direct pulmonary insults, such as severe lung contusion, and nondirect insults, such as multiple extremity injuries and long bone fractures, systemic inflammation and infections, have been described.[2] It is characterized by increased permeability, presence of pulmonary edema and respiratory dysfunction.[2] The influence of the initial management on the incidence of ARDS has been confirmed in many studies and imply the correction of pathological conditions, such as protocols for resuscitation,[3,4] chest injuries,[5] and coagulopathy.[6] Also, soft tissue and fracture management appear to play a role.[7] Orthopedic literature indicates that the timing of surgery may have possible relationship with ARDS.[7] In addition, patient age and associated comorbidities influence the mortality associated with pulmonary failure.[8] Our group has also looked at the issue of the quality of detection of pulmonary contusions, timing of major primary and secondary surgeries.[9] A scoring system developed on the basis of a large data base takes cofactors into account, such as age and physiologic changes.[9] Recently, several reports stated that the mortality rates of ARDS are decreasing and postulated that ARDS may no longer be a threat.[10,11] Others speculated about further cofactors, such as geographical distribution. Several publications pointed out differences of ARDS incidence in Europe and North America. Authors postulated that trauma system, differences in management of trauma patients, or even higher rates of smoking or a difference in genetic predisposition toward ARDS, might contribute to these differences.[7] To date, no scientific evaluation has been performed to support these assumptions in patients with severe blunt trauma. Several meta-analyses have focused on treatment issues

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for ARDS.[12] However, they have been inconclusive in terms of the optimal respiratory management, volume replacement, and other treatment options.[13]

We therefore performed a systematic review and meta-analysis in patients with posttraumatic ARDS to address some of the open questions addressed above. Specifically, we aimed at answering the following questions: (1) Has there been a change in the incidence of posttraumatic ARDS over the past decades? (2) Are any geographical influences discernible within western societies? (3) Is the type of surgical service related to the rate of ARDS?

We hypothesize that the incidence of ARDS has changed over the last three decades. Moreover, we hypothesize that there is no difference of ARDS incidence between European and North American publications and articles published by responsible surgical subspecialties (general surgeons and orthopedic trauma surgeons).

MATERIALS AND METHODS

Study Selection

Two authors (R.P., M.E.) independently reviewed all of the retrieved references by title and abstract, followed by full-text articles if the inclusion criteria were met. Studies were included if they were published between Jan 1, 1980, and December 31, 2015.

Disagreement between reviewers regarding the fulfilment of inclusion criteria were resolved by discussion. All abstracts were screened for information on the incidence of ARDS. If an article did not contain data on ARDS incidence, the full text was also screened to ensure a complete set of publications. Moreover, the references of all included studies were reviewed.

Data Items and Definitions

The following basic parameters were extracted from every publication: first author, date of publication, country of origin, study design (e.g., prospective vs. retrospective), number of patients included, patient demographics, lead clinical service of the main authors (orthopedic vs. general surgery), incidence of ARDS, and decade of patient enrolment. Three decades were separately reviewed according to the patient's recruitment reported in the publications (1980 to 1990 [decade 1], 1991 to 2000 [decade 2], and 2001 to 2010 [decade 3]). For classification of the reported study period into decades, the end of the reported recruitment period for patients for each study was used. Studies which reported results for different periods were included in the analysis as separate trials for each period.

The severity of injury was categorized in studies using the Injury Severity Score (ISS).[14] The severity of thoracic injuries was usually graded according to the admission chest x-ray, the chest x-ray at day 1 postadmission, and the chest computed tomography, if available.[15]

For this meta-analysis, adult respiratory distress syndrome was diagnosed according to the valid criteria at the time of diagnosis (Table 1). Based on previous definitions of ARDS, there appears to be widespread agreement on the definition of ARDS, as highlighted in a consensus conference between North America or Europe.[19] Based on this information and other background data, the geographic region was selected to differentiate Europe from North America.[7,58]

Surgical Background (General Surgery and Orthopedic Surgery)

The selection was based on two types of information:

1. Studies published by authors and co-authors from the given services
2. A main focus on orthopedic injuries/with leading orthopedic injuries (e.g. femoral fractures, etc.)

Depending on these criteria, they were defined as *orthopedic trauma* populations, while trials with leading general trauma injuries (e.g., abdominal trauma, etc.) were defined as *general trauma* population.

Protocol and Registration

Study inclusion criteria, primary outcome, and the method of statistical analysis were specified *a priori* in a review protocol. This study was performed and reported according to the Preferred Reporting Items for Systematic Reviews (PRISMA).[59] The PRISMA checklist[60] was used to ensure that all relevant information is included. No formal registration of the review protocol was taken.

Eligibility Criteria

We included randomised trials and observational studies reporting on posttraumatic Acute Respiratory Distress Syndrome (ARDS). Criteria for inclusion were as follows; English language, and multiply injured patients or patients with polytrauma treated at an intensive care unit (ICU), but selected population collectives (e.g., isolated thoracic trauma) and nontrauma studies were excluded.

Information Sources and Searches

We performed an electronic literature search of PubMed, MEDLINE, and ISI Web of Knowledge using relevant keywords, including "acute respiratory distress syndrome," "ARDS," "multiple trauma," "polytrauma," and "surgery." We restricted our search to articles in English language. The search was difficult due to the fact that ARDS incidence was not the main focus of the published studies. Therefore, we decided to perform a broad search to avoid overlooking potential relevant studies. In addition to the database search, experts in the field of trauma surgery were asked for potentially relevant studies.

Data Collection Process

Previously defined parameters were extracted independently by two authors (R.P., M.E.) and documented in an Excel sheet. A cross-check of the extracted data was performed by all authors. Any disagreement was resolved by a consensus discussion in personal meetings of all authors.

Risk of Bias

The methodological quality assessment of each study included was performed according to the risk of bias tool[61,62] by one author (R.P., E.M.). This includes the assessment of adequacy of randomisation, concealment, and blinding and the evaluation of incomplete outcome data, as well as the susceptibility of selective reporting.

TABLE 1. List of Studies Included Into the Systematic Review

ID	Study	n	no_of ARDS Events	ARDS_rate	Inclusion Criteria	Group	Decade	Region	Study Design	ARDS Definition	Risk of Bias
1	Regel 1995a[16]	1,703	310	0.18203	Multiple trauma	General	1	EU	Retrospective cohort study	Regel et al.[16,17]	Unclear
2	Regel 1995b[16]	1,703	205	0.12038	Multiple trauma	General	2	EU	Retrospective cohort study	Regel et al.[16,17]	Unclear
3	Navarrete-Navarro 2000[18]	636	59	0.09277	All trauma	General	2	EU	Prospective cohort study	AECC[19]	Low
4	Navarrete-Navarro 2001a[20]	5,708	486	0.08514	All trauma	General	1	EU	Prospective cohort study	AECC[19]	Low
5	Navarrete-Navarro 2001b[20]	12,706	552	0.04344	All trauma	General	2	EU	Prospective cohort study	AECC[19]	Low
6	Miller 2002[21]	4,397	200	0.04549	Blunt trauma	General	2	NAM	Retrospective cohort study	AECC[19]	Low
7	Johnston 2003[22]	4,020	484	0.12040	All trauma	General	2	NAM	Prospective cohort study	AECC[19]	Low
8	White 2004[23]	7,192	36	0.00501	All trauma	General	2	EU	Prospective cohort study	AECC[19]	Low
9	Dicker 2004[24]	254	70	0.27559	Multiple trauma + intubated	General	3	NAM	Prospective cohort study	AECC[19]	Low
10	Treggiari 2004[25]	1,296	154	0.11883	All trauma + ICU	General	2	NAM	Prospective cohort study	AECC[19]	Low
11	Martin 2005[26]	1,913	274	0.14323	All trauma + ICU	General	3	NAM	Prospective cohort study	AECC[19]	Low
12	Ciesla 2005[27]	1,344	437	0.32515	All trauma + ∅ BI	General	3	NAM	Prospective cohort study	AECC[19]	Unclear
13	Salim 2006[28]	2,042	216	0.10578	All Trauma ICU	General	3	NAM	Retrospective case–control study	AECC[19]	Low
14	Plurad 2007[29]	2,346	192	0.08184	All trauma + ventilation	General	3	NAM	Retrospective cohort study	AECC[19]	Low
15	Chaiwat 2009[30]	14,070	512	0.03639	All trauma + AIS ≥ 3	General	3	NAM	Prospective cohort study	AECC[19]	High
16	Watson 2009[31]	1,175	306	0.26043	All trauma + BT	General	3	NAM	Prospective cohort study	AECC[19]	Low
17	Shah 2010[32]	280	90	0.32143	All trauma + ∅ BI with AIS ≥ 3	General	3	NAM	Prospective cohort study	AECC[19]	High
18	Plurad 2011[33]	43,664	2260	0.05176	All trauma + Level I + II + III hospitals	General	3	NAM	Retrospective cohort study	AECC[19]	Unclear
19	Mommsen 2011[5]	278	60	0.21583	Trauma + TT + ∅ BI	General	3	EU	Retrospective cohort study	AECC[19]	High
20	Strumwasser 2011[34]	106	12	0.11321	Trauma + lung contusion	General	3	NAM	Retrospective cohort study	AECC[19]	High
21	DuBose 2011[35]	3,465	437	0.12612	Trauma with VAP	General	3	NAM	Retrospective cohort study	AECC[19]	High
22	Andrews 2013[36]	231	3	0.01299	Trauma ISS >16 + FF	General	3	NAM	Retrospective cohort study	AECC[19]	Unclear
23	Goris 1982[37]	58	17	0.29310	All trauma	Ortho	1	EU	Retrospective cohort study	Goris et al[37]	High
24	Talluci 1983[38]	100	6	0.06000	All trauma + nailing	Ortho	1	NAM	Retrospective cohort study	Talluci et al[38]	Unclear
25	Johnson 1985[39]	132	25	0.18939	All trauma + fractures	Ortho	1	NAM	Retrospective cohort study	Goris et al[37,40]	High
26	Bone 1989[41]	83	7	0.08434	All trauma + FF	Ortho	1	NAM	Randomized clinical trial	Bone et al[41]	Low
27	Behrman 1990[42]	339	7	0.02065	All trauma + FF	Ortho	1	NAM	Retrospective cohort study	Behrmann et al[42]	Low
28	Poole 1992[43]	71	4	0.05634	All trauma + BI + FF	Ortho	1	NAM	Retrospective cohort study	Poole et al[43]	High

Continued next page

TABLE 1. *(Continued)*

ID	Study	n	no_of ARDS Events	ARDS_rate	Inclusion Criteria	Group	Decade	Region	Study Design	ARDS Definition	Risk of Bias
29	Pape 1993[44]	50	10	0.20000	All trauma with ISS > 16 + FF	Ortho	1	EU	Retrospective cohort study	Pape et al[44]	Low
30	Charash 1994[45]	82	4	0.04878	Multiple trauma + FF	Ortho	2	NAM	Retrospective cohort study	Charash et al[45]	Low
31	Friedl 1996[46]	55	8	0.14545	All trauma with ISS >15 + fractures	Ortho	2	EU	Retrospective cohort study	AECC[19]	High
32	Boulanger 1997[47]	83	6	0.07229	All frauma ISS ≥16+ FF	Ortho	2	NAM	Retrospective cohort study	ND	Unclear
33	Starr 1998[48]	17	0	0.00000	All trauma + FF + BI	Ortho	2	NAM	Retrospective cohort study	Murray JF[49]	High
34	Brundage 2002[50]	516	52	0.10078	All trauma ISS >15 + FF	Ortho	2	NAM	Retrospective cohort study	ND	Low
35	Pape 2002a[51]	235	160	0.68085	All trauma ISS >18+ FF	Ortho	2	EU	Retrospective cohort study	AECC[19]	Low
36	Pape 2002b[51]	191	48	0.25131	All trauma ISS >18+ FF	Ortho	3	EU	Retrospective cohort study	AECC[19]	Low
37	Pape 2007[52]	165	15	0.09091	All trauma NISS >16 + fractures	Ortho	3	EU	Randomized clinical trial	AECC[19]	Low
38	Wang 2007[53]	96	7	0.07292	Multiple trauma + BI + fractures	Ortho	3	NAM	Retrospective cohort study	ND	Unclear
39	O-Toole 2009[7]	227	3	0.01322	All trauma + FF	Ortho	3	NAM	Retrospective cohort study	AECC[19]	High
40	Lefaivre 2010[54]	1,958	28	0.01430	All trauma + FF	Ortho	3	NAM	Retrospective cohort study	AECC[19]	Low
41	Scannell 2010[55]	145	6	0.04138	All trauma NISS >16 + FF	Ortho	3	NAM	Retrospective cohort study	AECC[19]	Unclear
42	Harvin 2012[56]	1,376	15	0.01090	All trauma + FF	Ortho	3	NAM	Retrospective cohort study	ND	High
43	Vallier 2013[57]	1,443	33	0.02287	All trauma + fractures	Ortho	3	NAM	Retrospective cohort study	AECC[19]	Low

ND, no data; EU, European studies; NAM, North American studies; BI, brain injury; AIS, Abbreviated Injury Score; BT, blood transfusion; TT, thoracic trauma; VAP, ventilation-associated pneumonia; FF, femur fracture.

Statistics

Summary Measures

The primary outcome measure in this study was the incidence of ARDS. For each study a single proportion for the occurrence of ARDS was computed. Those studies that reported results for more than one group in different periods were included in the analysis as separate trial for each period. For each trial, the proportion of ARDS patients with the corresponding 95% confidence interval was derived as log-odds and back-transformed to the original scale using the inverse logit transformation.

Synthesis of Results

A pooled estimate of the mean log-odds of ARDS and corresponding 95% confidence interval was calculated by random-effects logistic regression model (binomial-normal model) to allow for heterogeneity in the analysis. The median incidence of ARDS and its confidence interval was calculated by transforming the mean log-odds and its confidence interval back into the probability scale.[63]

The Q-test was used to assess statistical heterogeneity between studies at a significance level of 10%. Additionally, the I^2 was calculated to describe the amount of inconsistency of findings across studies.

Additional Analyses

To evaluate potential moderators, univariate meta-regressions were performed for each potential differentiating factor. The following factors were considered at the study level and included as effect modifiers in a logistic regression model with random intercept:

1. The period of patient recruitment for each study categorized in decades from 1980 to 1990 (decade 1), 1991 to 2000 (decade 2), and 2001 to 2010 (decade 3) according to the end of recruitment for each study;
2. The type of admitting service was categorized as orthopedic or general trauma population; and
3. Geographical region was subdivided between Europe and North America;
4. All analyses were carried out using R (version 3.1.2, metafor package[64]).

RESULTS

Study Selection

Among the 40 publications identified, 43 trials (three studies[16,20,51] reported on two different decades, respectively) were included in this systematic review. Figure 1 documents a flowchart of the study selection process. The initial search provided 715 potentially relevant studies. After the review of titles and abstracts, 630 studies were excluded due to the inclusion criteria.

All full texts of the remaining 85 studies were submitted to a detailed examination. Subsequently, 45 additional studies were excluded because they described the examination of multiply injured patients, whereas they included isolated fracture patients, nontrauma patients (23) or selected other patient populations (11). In six other studies, no data regarding ARDS was presented. Furthers reasons were the inclusion of only patients with ARDS (2), and double reporting of the same population as in previous publications from the same group (3). If the ARDS incidence was reported across different decades or if the service was inconclusive within one publication, the study was divided into separate trials according to the criteria indicated by the authors. This applied to three studies, thus leaving 40 studies (43 trials) for inclusion.

Study Characteristics

Among the 40 studies included in this meta analysis, 11 represented a prospective cohort-study, 27 were retrospective studies, and two were randomized controlled trials.

This meta-analysis summarizes 117,951 patients, among which 7,816 were diagnosed with posttraumatic ARDS. Two publications[24,35] did not report a defined study period and were

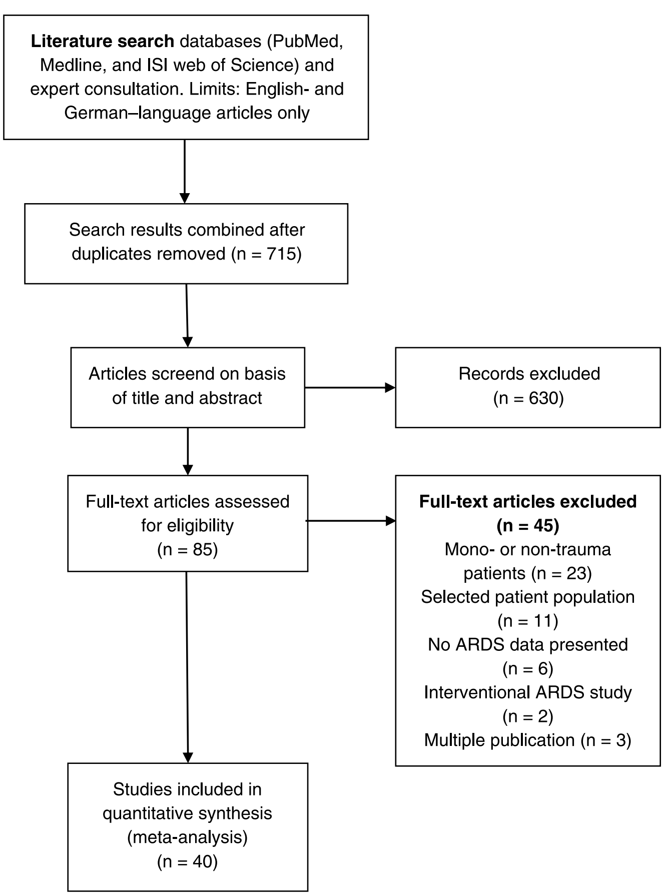

Figure 1. Flow diagram of studies included.

assigned based on the following criteria. Dickers et al. used definitions from 2003, and DuBose et al[16] included data from the National Trauma Database > 2011. Therefore, both studies were assigned to the third decade. In the study of Regel et al. ARDS rates for two different decades were reported. To avoid double counting, the total number of patients was divided in half for each decade, because the absolute number of patients was not mentioned in the article.

The regional assignment was made if data were reported to derive from North America (United States and Canada). Chaiwat et al.[30] did not mention a particular region of origin, but summarized data from National Centres in the United States. Assignment to Europe was done if data were derived from the European Union, Israel, Switzerland and Ukraine.

Results of Individual Studies

The incidence of ARDS and the risk of bias was categorized for each study; the results are presented in Table 1.

Incidences of ARDS Incidences Over Time

The overall median ARDS incidence was 8.4% (n = 43; 95% CI, 6.0–11.6%). Heterogeneity between trials was considerable (I^2 = 99.50%, Q-test $p < 0.0001$).

The estimated median incidence of ARDS in decade 1 (nine trials) was 10.4 (95% CI, 6.1–17.1% I^2 = 97.22%, Q-test $p < 0.0001$). In decade 2, the median ARDS incidence summarized 13 trials and revealed an incidence of 7.7% (95% CI, 3.8–15.1%, I^2 = 99.49%, Q-test $p < 0.0001$). In decade 3, the median estimated ARDS incidence based on 21 trials was 8.0% (95% CI, 4.9–12.9%, I^2 = 99.58, Q-test $p < 0.0001$ (Table 2, Fig. 2). Meta-regression showed no significant difference ($p = 0.8322$).

Assessment of Possible Geographical Differences

Among the 30 North American studies, 28 were conducted in the United States and 2 in Canada. The estimated median incidence of ARDS in North America was 6.9% (95% CI, 4.8–9.9%, I^2 = 99.36%, Q-test $p < 0.0001$).

Among the 10 European studies, five were from Germany, two from Spain, and one each from the United Kingdom, Netherlands, and Switzerland, respectively. The estimated median incidence of all 13 studies was 13.0% (95% CI, 6.7–23.7%), I^2 = 99.49%, Q-test $p < 0.0001$. Thus, geographical observations revealed no significant difference ($p = 0.0696$) (Table 2, Fig. 3).

Comparison of Services (Orthopedic Surgery versus General Surgery)

The estimated median incidence of ARDS of the general trauma population was 9.8% (95% CI, 6.5–14.5%; I^2 = 99.67%, Q-test $p < 0.0001$), in 22 trials (Table 2), and 7.0% (95% CI, 4.0–11.8%; I^2 = 96.02%, Q-test $p < 0.0001$) in 21 trials in the orthopedic trauma population ($p = 0.3436$ according to meta-regression) (Table 2, Fig. 4). Supplement 1 depicts the clinical data for both study populations (see Supplemental Digital Content 1, http://links.lww.com/TA/A971).

DISCUSSION

ARDS continues to represent a life-threatening medical condition, characterized by significant morbidity and high

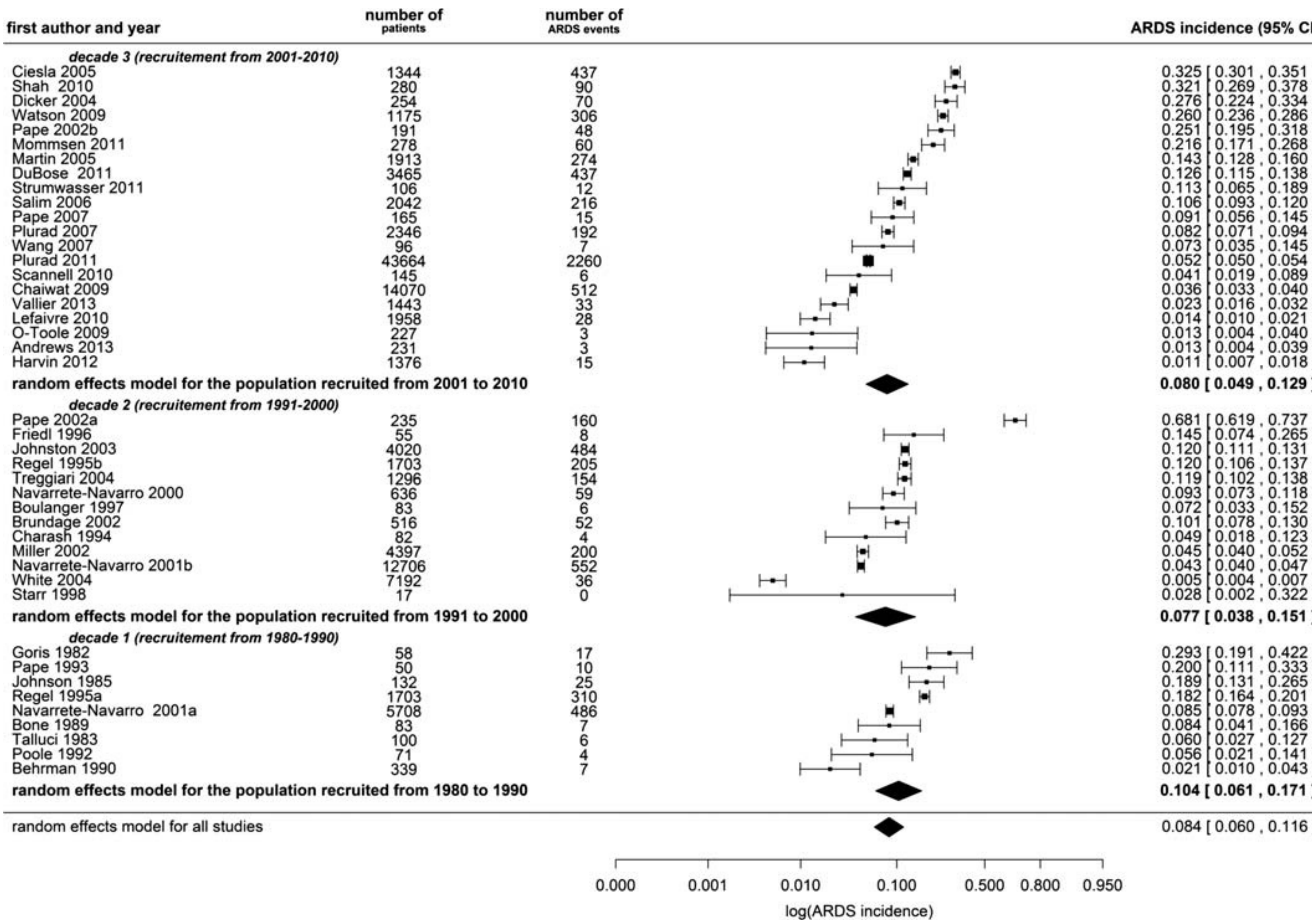

Figure 2. Meta-analysis of the literature according to the timepoint of publication over the last three decades.

in-hospital costs.[15,65,66] In a recent clinical study of 29,444 ICU patients, the incidence of ARDS induced by trauma was 4.2 %, but the mortality continued to represent an issue.[10] Among patients suffering from ARDS, trauma-induced pulmonary failure is a special entity, because it occurs in younger individuals, is frequently induced by a lung contusion and is associated with instability of the rib cage, such as serial rib fractures and flail chest. The latter conditions may be the source of prolonged hypoventilation. Also, it can be caused by a second hit phenomenon, for example, local or systemic infection.[67,68]

TABLE 2. Meta-Analysis of the Literature According to the Timepoint of Publication, Attributable to Geographic Distribution, and Related to Admitting Surgical Subspecialities

Description of Data				Results of Meta-analysis		
Group	**No. Studies***	**No. Patients**	**No. Patients With ARDS**	**Estimate of Incidence (95% CI)**	**I^2**	**p Value for the Comparison of Groups**
General trauma	22	110,529	7,355	9.8% (6.5–14.5%)	99.67%	0.3436
Orthopedic trauma	21	7,422	461	7.0% (4.0–11.8%)	96.02%	
Total	43	117951	7,816	8.4% (6.0–11.6%)	99.50%	
Decade 1	9	8244	872	10.4 (6.1–17.1%)	97.22%	0.8322
Decade 2	13	32938	1,920	7.7% (3.8–15.1%)	99.49%	
Decade 3	21	76,769	5,024	8.0% (4.9–12.9%)	99.58%	
Total	43	117,951	7,816	8.4% (6.0–11.6%)	99.50%	
EU	13	30,680	1,966	13.0% (6.7–23.7%)	99.49%	0.0696
NAM	30	87,271	5,850	6.9% (4.8–9.9%)	99.36%	
Total	43	117,951	7,816	8.4% (6.0–11.6%)	99.50%	

*Three publications contain two studies each (Regel 1995a/b; Navarette-Navarro 2001a/b; and Pape 2002a/b).

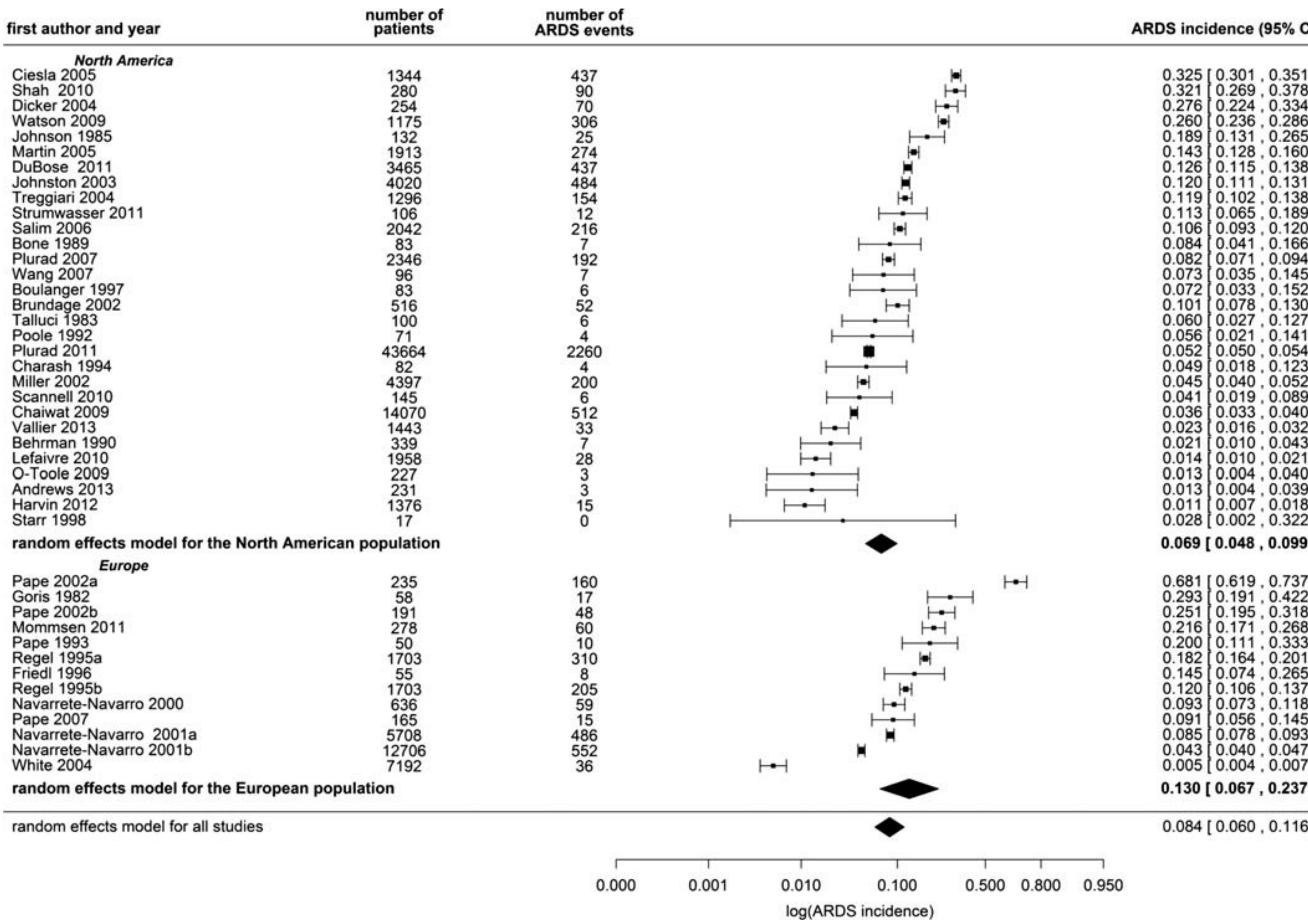

Figure 3. Meta-analysis of the literature according to geographic location of publications.

To our knowledge, none of these cofactors have been studied in detail. We therefore feel that a meta-analysis on posttraumatic ARDS is justified, and the results obtained differ from those obtained from ARDS without traumatic origin, such as described in internal medicine patients. These frequently have other underlying causes, such as chronic obstructive pulmonary disease, cardiac disease, and pulmonary infection.[2,67,69] Several of these causes may occur in trauma patients as well, because these represent an ageing population.[69]

The current meta-analysis is based on all available clinical studies that dealt with posttraumatic ARDS. The results can be summarized as follows:

1. There was no trend in the incidence of trauma-induced ARDS across the three decades observed.
2. No significant geographical difference in the incidence of posttraumatic ARDS was found when comparing North American and European countries.
3. Publications that derive from a general surgery service demonstrated comparable ARDS incidence as those summarized in publications from orthopedic surgeons

Several shortcomings of this analysis should be considered:

First, there have been changes in the definition of ARDS over time. Although the initial description by Ashbaugh et al.[70] served to separate pulmonary edema from cardiogenic edema, different definitions have been described (American/European Consensus Conference [AECC]) and a subentity called Acute lung injury.[19,71] To address this issue, a sensitivity analysis based on studies with AECC definition of ARDS (n = 28) was performed (see Table S2, Supplemental Digital Content 1, http://links.lww.com/TA/A971). There was neither a change in the incidence over the last decades nor a geographical difference within western societies, nor associated with the admitting surgical subspeciality. Second, the separation between patients treated by a general surgery service and orthopedics is surprising. It is of note that the trauma system involved may affect the mode of documentation for both services. We tried to account for this influence by considering several factors. We assessed the affiliations of all coauthors, not just the first author. In addition, for those where the affiliation did not appear to be clear, a review was performed on whether previous publications provided a hint. Third, the influence of a trauma system was considered, as reviewed previously.[72]

Finally, there has been considerable statistical heterogeneity between the studies included in the analysis. We expected a sustained clinical heterogeneity between studies because of diverging aims. To account for this effect, we used a random-effects model reflecting the uncertainty in estimating the

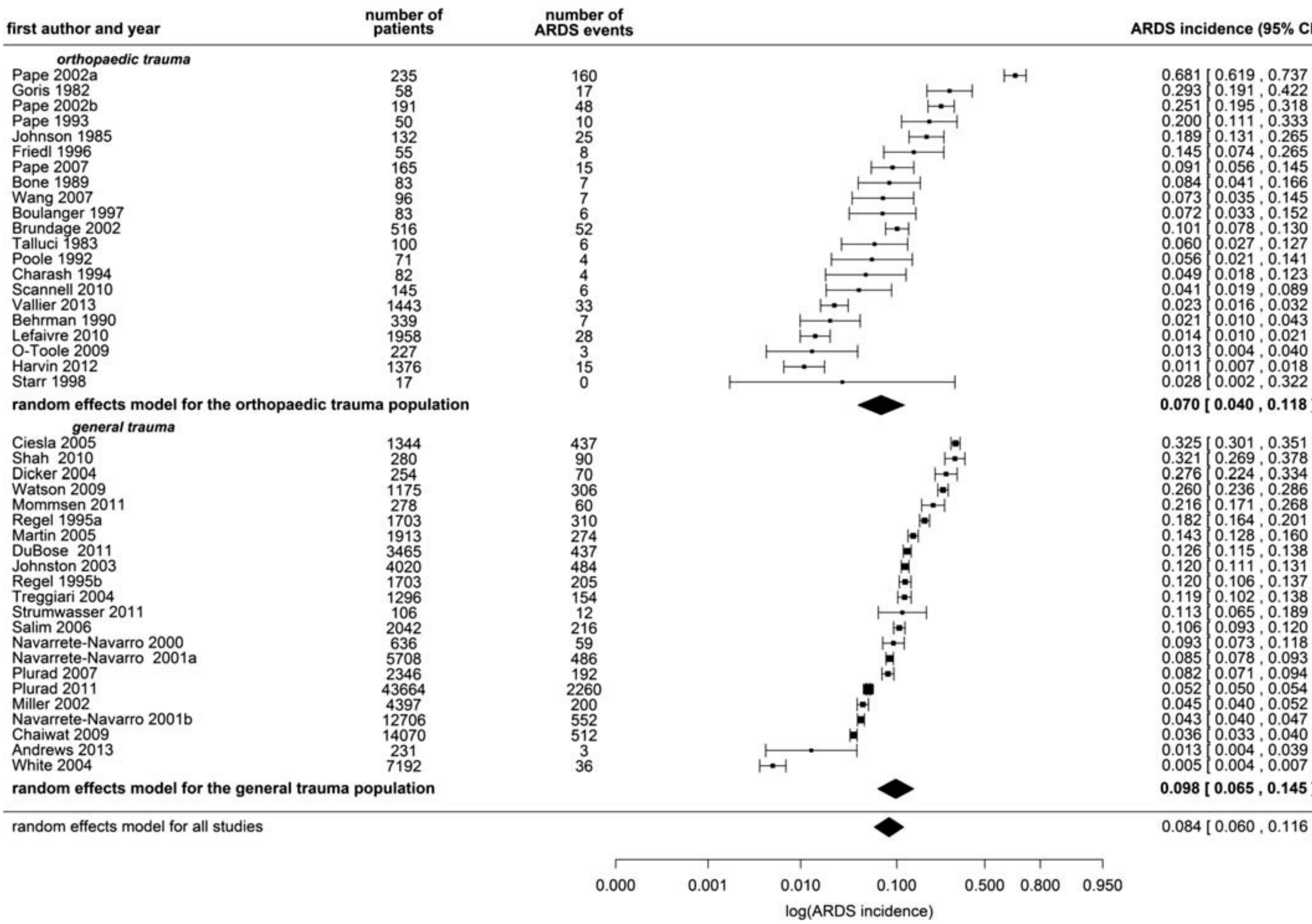

Figure 4. Meta-analysis of the literature according to admitting surgical subspecialities.

summary effects. Moreover, we prespecified different subgroup analyses to explore possible causes of clinical heterogeneity. However, despite the obvious candidate moderators, the period of patient recruitment, the geographical region, or the type of trauma were unable to explain the statistical heterogeneity between studies. Statistical heterogeneity was substantial and ranged between 96.02% and 99.67% in the specific subgroups. On the one hand, this heterogeneity may be due to the versatile study populations caused by different aims of the respective studies. On the other hand, the observed heterogeneity neither interferes with the quality nor with the validity of the results obtained.

The lack of change in the incidence of ARDS is unexpected, because several reports had indicated an improved outcome related to pulmonary complications. Some of them even state that the clinical threat of ARDS no longer represents a sustained complication.[7,73,74] This appeared to be the case in particular in the orthopedic literature.[26,29] A change in resuscitation protocols was discussed to be a cause.[7] Undoubtedly, resuscitation strategies have changed, and modalities of diagnostics have improved over time. It has been discussed that these changes were associated with an alteration in mortality. The consequences on the ARDS incidence were not described so far. Although legislative improvements and those regarding active and passive car safety[75] should have contributed to a lower ARDS incidence, such an effect was not found in the current study. It is possible that more severely injured patients with high ISS might survive the initial stages of trauma and develop their complications, such as ARDS, during the further course. Also, more elderly patients — known to be eligible for ARDS — sustain a severe injury.[76]

Differences in the incidence of ARDS in European and North American studies have been discussed in previous publications.[69,77,78] Preclinical rescue concepts (scoop and run versus stay and play) were discussed, as trauma systems are variable.[72] Also, resuscitation protocols may vary between European and North American centres,[69] and peri-operative management.[7,79] Finally, patient factors, such as high rates of smoking, genetic predisposition, and more severe lung injury, have been discussed in the past.[7] Treatment algorithms of major fractures may also play a role. It has been hypothesized that the inadequate timing of major surgeries influences the clinical course.[80] In this line, a matched-pair analysis about the timing of major fracture fixation and systemic complications in large trauma centers in Europe and United States of America revealed no differences in the timing of definitive fracture care.[81] The overall incidence of ARDS (Germany, 12.5% and US, 13.4%) in both study groups was comparable. The results of our analysis, which includes 30 North American studies and 13 European publications, are in line with this publication and discards that a difference in the incidence of ARDS incidence occurs in comparison between European and North American trials.

To include previously undiscussed factors influencing the results of published studies, we distinguished between studies published by general surgeons versus those published by orthopedic trauma surgeons. In some North American trauma systems, the decision to clear the trauma patient for emergency interventions is usually made by general surgeons. In some European countries, the role of the orthopedic surgeon is close to that of general surgeons in North America (Netherlands, Switzerland, United Kingdom). In others, ICU physicians work in close cooperation with surgical disciplines (Spain). We have tried to account for the fact that surgical ICUs are usually assigned to general surgeons as well. However, we were unable to find the information in the published studies. In some of them, detailed information about the course of intensive care was missing, in others the focus of general complications was set for ARDS only, and there was no mention about other complications relevant to the clinical stay ((multi organ dysfunction syndrome), sepsis, and mortality).

We expected to find a higher ARDS incidence in patients treated by general surgery service due to the fact that these patients more frequently sustained truncal injuries (thoracic and abdominal trauma). The majority of studies by general surgeons provided a detailed description for all truncal injuries known to be associated with severe blood loss and related systemic consequences, such as SIRS, sepsis, or ARDS.[82,83] In comparison, articles published by orthopedic trauma surgeons more frequently focus on pelvic and extremity injuries. Despite the possible selection bias in both surgical disciplines, we did not observe any significant differences in ARDS incidence (9.8% vs. 7.0%). We also compared the ISS and rates of thoracic and abdominal trauma published in both groups (see Supplemental Digital Content 1, http://links.lww.com/TA/A971). Our patient subset demonstrated no difference in injury severity and reported that frequency of truncal injuries showed high variation. We are aware of the limitation of the ISS, which is an anatomically based scoring system neglecting physiologic parameters.[84] Consequently, the injury pattern and patients physiology might be still different between the studies. Moreover, surgical strategies (damage control surgery versus early total care) may also influence the outcome and incidence of systemic complications, such as ARDS.[85] This subanalysis was not the focus of this meta-analysis and need to be further studied.

CONCLUSION

In conclusion, this meta-analysis demonstrates that the incidence of trauma-induced ARDS has not changed over the last few decades, and ARDS is not related to a geographic region, as mentioned above, nor does it vary according to a surgical subspecialty. Other factors may play a role, such as pneumonia or ventilation, which result in the ongoing threat of pulmonary failure in trauma patients. Finally, another future direction is to analyze the role of different ARDS definition on published incidence.

AUTHORSHIP

R.P. contributed to the conception of the study and interpretation of the data, participated in the acquisition and critical appraisal of data, drafted the article and revised it critically, and agreed to the final version of the article and to be accountable for all aspects of the work. N.H. contributed to the statistical design of the study and the statistical analysis and interpretation of the data, drafted the statistical part of the article and revised the article critically, and agreed to the final version of the article and to be accountable for all aspects of the work. E.M. contributed to the acquisition and critical appraisal of data, and agreed to the final version of the article and to be accountable for all aspects of the work. R.D.H. contributed to statistical interpretation of the data and revised the article critically, and agreed to the final version of the article and to be accountable for all aspects of the work. H.C.P. contributed to the conception of the study and interpretation of the data, drafted the article and revised it critically, and agreed to the final version of the article and to be accountable for all aspects of the work.

DISCLOSURE

The authors declare no conflicts of interest.
R.P. and N.H. contributed equally.
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